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2.7.1.37.AGC

1 Nomenclature

EC number

2.7.1.37.AGC (Protein kinases are in a state of review by the NC-IUBMB. This EC class will presumably be split up into EC 2.7.11.11, EC 2.7.11.12, EC 2.7.11.13, EC 2.7.11.14, EC 2.7.11.15, EC 2.7.11.16)

Systematic name

ATP:protein phosphotransferase

Recommended name

protein kinase (PKA, C, AKT, GRK, AGC-related, RSK, DBF2,)

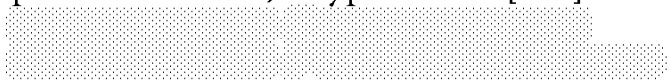
3-phosphoinositide dependent protein kinase-1 <4, 98, 102> [4, 179, 180]
AKT kinase transforming protein <178> [340]
AKT1 <113> [192]
AKT2 <180> [342]
ARK <44> [99]
Akt protein kinase <113> [187]
Akt-3 <114> [227]
Akt2 <267> [480]
Akt3 <114> [226]
Capkc1p <204> [381]
DG1 protein kinase <66> [130]
DM kinase <248> [419]
DM-kinase <229> [420]
DMPK <229> [418]
EC 2.7.1.125 (high sequence-similarity to cAMP-dependent protein kinases and protein kinase C)
EC 2.7.1.126 (high sequence-similarity to cAMP-dependent protein kinases and protein kinase C)
G protein-coupled receptor kinase 1 <184> [348]
G protein-coupled receptor kinase 2 <185> [247, 348, 349]
G protein-coupled receptor kinase GRK4 <181> [344, 345, 346]
G protein-coupled receptor kinase GRK5 <191> [362]
G protein-coupled receptor kinase GRK5 <205> [382]
G protein-coupled receptor kinase GRK5 <270> [484]
G protein-coupled receptor kinase GRK6 <206> [383]
G protein-coupled receptor kinase GRK6 <233> [428]
G protein-coupled receptor kinase GRK7 <115> [189]
GRK5 <191> [362]

GRK5 <205> [382]
GRK6 <206> [383, 384]
GRK7 <115> [189]
Gprk2 <185> [349]
ISPK-1 <216> [399]
MT-PK <248> [449]
NPH1 <125> [244]
PAK-1 <272> [486]
PDK1 <98> [179]
PICK1 <164> [308]
PKC Apl I <260> [471]
PKC Apl II <261> [474]
PKC δII <110> [191]
PKC δIII <145> [286]
PKC ι <202> [377]
PKC λ <268> [481]
PKC ζ <122> [241]
PKC-L <174> [336]
PKC-δ <244> [440]
PKC-ε <158> [302]
PKC-zeta <137> [268]
PKC1B <190> [361]
PKCδ <145> [287]
PKC ν <133> [257]
PKD2 <116> [190]
RAC-PKγ <273> [487]
RAC-α serine/threonine kinase <113> [187, 192, 220, 221, 222, 223, 224]
RAC-α serine/threonine kinase <236> [222]
RAC-α serine/threonine kinase <179> [341]
RAC-α serine/threonine kinase <210> [390]
RAC-β serine/threonine protein kinase <180> [342, 343]
RAC-β serine/threonine protein kinase <211> [390]
RAC-β serine/threonine protein kinase <267> [480]
RAC-γ serine/threonine protein kinase <114> [188, 225, 226, 227, 228]
RAC-γ serine/threonine protein kinase <286> [225]
RAC-γ serine/threonine protein kinase <273> [487]
RAC/Akt kinase <113> [221]
RSK3 <255> [463]
ribosomal protein S6 kinase α 1 <274> [488]
Rsk-1 S6 kinase <274> [488]
S6K2 <283> [497]
S6KII α <149> [293]

α-PKC <164> [309]
β-adrenergic receptor kinase <38> [90]
β-adrenergic receptor kinase 1 <44, 47, 89> [98, 99, 100, 101, 104, 105, 167]
β-adrenergic receptor kinase 2 <48, 49, 59> [104, 106, 119, 120]

cAMP-dependent protein kinase <1> [1]
cAMP-dependent protein kinase catalytic subunit <27, 37, 58, 61, 62> [3, 67, 68, 69, 89, 116, 117, 118, 122, 123, 124]
cAMP-dependent protein kinase type 1 <15> [30, 32, 33]
cAMP-dependent protein kinase type 2 <16> [30, 34, 35]
cAMP-dependent protein kinase type 3 <14> [29, 30, 31]
cAMP-dependent protein kinase, α-catalytic subunit <8, 52> [12, 13, 14, 15, 16, 108]
cAMP-dependent protein kinase, α-catalytic subunit <34, 45, 100> [26, 84, 85, 86, 180]
cAMP-dependent protein kinase, β-1 catalytic subunit <11> [24]
cAMP-dependent protein kinase, β-2-catalytic subunit <9> [17]
cAMP-dependent protein kinase, β-catalytic subunit <12, 13> [25, 26, 27, 28]
cAMP-dependent protein kinase, β-catalytic subunit <41> [93]
cAMP-dependent protein kinase, γ-catalytic subunit <40> [93, 94]
cAPK <58> [116]
cGK <73> [140]
cGK II <88> [166]
cGMP-dependent protein kinase 1, α isozyme <6, 7, 73> [6, 7, 8, 9, 10, 11, 77, 140]
cGMP-dependent protein kinase 1, β isozyme <30, 36, 97> [11, 77, 78, 88, 178]
cGMP-dependent protein kinase 2 <70, 84, 88> [133, 134, 135, 161, 166]
cGMP-dependent protein kinase, isozyme 1 <66> [67, 115, 130]
cGMP-dependent protein kinase, isozyme 2 forms cD5/T2 <57> [115]
calcium dependent protein kinase C
calcium-dependent protein kinase C <260> [471, 472, 473]
calcium-independent protein kinase C <261> [471, 472, 473, 474, 475]
calcium/phospholipid dependent protein kinase
cell cycle protein kinase DBF2 <167> [316, 317]
guanosine cyclic 3',5'-phosphate dependent protein kinase <7> [10]
heart muscle protein kinase
insulin-stimulated protein kinase <216> [399]
myotonic dystrophy protein kinase <229> [418, 419, 420, 421]
myotonin-protein kinase <229> [418]
myotonin-protein kinase <248> [419, 421, 449, 450, 451, 452, 453, 454]
nPKC eta <170> [326]
nPKC theta <238> [433]
nonphototropic hypocotyl protein 1 <125> [243, 244, 245, 246]
p54 S6 kinase 2 <283> [497]
p70 S6 kinase <165> [311]
p70 S6 kinase <283> [499]
p70(S6k) <165> [311]
phosphatidylserine-sensitive calcium-dependent protein kinase
phototropin <125> [244]
pp90rsk Ser/Thr kinase <255> [463]
protein kinase 2 <175> [337]

protein kinase A
protein kinase B α <113> [221]
protein kinase B γ <286> [225, 228]
protein kinase Bγ <114> [228]
protein kinase C
protein kinase C <156> [247, 299]
protein kinase C α <160> [305]
protein kinase C δ <110> [191]
protein kinase C δ <145> [286]
protein kinase C, D2 type <116> [190, 229]
protein kinase C, α type <135> [263, 264]
protein kinase C, α type <139> [263, 270, 271]
protein kinase C, α type <148> [263, 281]
protein kinase C, α type <160> [304, 305]
protein kinase C, α type <164> [308, 309, 310]
protein kinase C, β type <109> [183, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208]
protein kinase C, β type <136> [263, 265]
protein kinase C, β type <141, 142> [275, 276, 277, 278, 279, 280, 281]
protein kinase C, brain isoenzyme <138> [247, 269]
protein kinase C, δ type <110> [184, 191, 209, 210, 211, 212]
protein kinase C, δ type <145> [286, 287, 288, 289, 290, 291]
protein kinase C, δ type <244> [440, 441]
protein kinase C, ε type <146> [290, 291]
protein kinase C, ε type <152> [295]
protein kinase C, ε type <158> [301, 302]
protein kinase C, ε type <239> [434]
protein kinase C, η type <170> [326]
protein kinase C, η type <174> [334, 335, 336]
protein kinase C, η type <275> [489]
protein kinase C, γ type <140> [208, 270, 272, 273, 274]
protein kinase C, γ type <137> [265, 266, 267, 268]
protein kinase C, γ type <151> [294]
protein kinase C, ι type <202> [376, 377]
protein kinase C, ι type <268> [481]
protein kinase C, μ type <254> [462]
protein kinase C, μ type <269> [482, 483]
protein kinase C, ν type <133> [257]



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protein kinase C, ζ type <243> [268, 439]
protein kinase C, ζ type <147> [290, 291, 292]
protein kinase C, ζ type <241> [436]
protein kinase C-ε <239> [434]
protein kinase C-η <275> [489]
protein kinase C-like <234> [429]

protein kinase C-like <278> [429]
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protein kinase C-like 1 <189> [359, 360]
protein kinase C-like 1 <204> [381]
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protein kinase C-like 2 <194> [182, 364, 365, 366]
protein kinase C-like 2 <259> [334, 469]
protein kinase C-like 2 <190> [361]
protein kinase Cδ <110> [184]
protein kinase Cδ <145> [287]
protein kinase C μ <269> [482]
protein kinase D <269> [483]
protein kinase D2 <116> [190]
protein kinase DBF20 <182> [316, 321]
protein kinase DC1 <33> [69]
protein kinase DC2 <159> [303]
protein kinase G
protein kinase HMK
protein kinase PKX1 <217> [401]
protein kinase PVPK-1 <157> [300]
protein kinase PrkC1
protein kinase SGK <111> [185]
protein kinase Sgk <107> [181]
protein kinase Ulc1
protein kinase x
rac-PK <180> [343]
rhodopsin kinase <53, 76, 86, 96> [109, 110, 146, 147, 148, 165, 177]
ribosomal S6 kinase (Rsk-2) <216> [396]
ribosomal protein S6 kinase <165> [311, 312, 313, 314]
ribosomal protein S6 kinase <171> [327]
ribosomal protein S6 kinase II α <149> [293]
ribosomal protein S6 kinase II α <161> [306]
ribosomal protein S6 kinase II β <150> [293]
ribosomal protein S6 kinase α 1 <162> [306]
ribosomal protein S6 kinase α 1 <256> [400]
ribosomal protein S6 kinase α 2 <255> [400, 463]
ribosomal protein S6 kinase α 2 <287> [501]
ribosomal protein S6 kinase α 3 <216> [396, 397, 398, 399, 400]
ribosomal protein S6 kinase α 6 <285> [500]
ribosomal protein S6 kinase β 2 <283> [497, 498, 499]
ribosomal protein S6 kinase β 2 <290> [504]
serine/threonine-protein kinase AtPK1/AtPK6 <203> [243, 378, 379, 380]
serine/threonine-protein kinase AtPK19 <265> [243, 378]
serine/threonine-protein kinase Pk61C <95> [67, 176]
serine/threonine-protein kinase SCH9 <23> [54, 55, 56]

serine/threonine-protein kinase Sgk <107> [181, 194, 195, 196]
serine/threonine-protein kinase Sgk <111> [185, 213, 214, 215, 216, 217, 218]
serine/threonine-protein kinase Sgk <288> [195]
serine/threonine-protein kinase Sgk <245> [196, 442, 443, 444, 445]
serine/threonine-protein kinase YPK1 <153> [296, 297]
serine/threonine-protein kinase YPK2/YKR2 <163> [296, 307]
serine/threonine-protein kinase cot-1 <198> [370]
serine/threonine-protein kinase nrc-2 <124> [242]
serine/threonine-protein kinase orb6 <2> [2]
serine/threonine-protein kinase sck1 <63> [3, 125]
spermatozoon associated protein kinase <166> [315]
type I β isozyme of cGMP-dependent protein kinase <30> [78]

CAS registry number

141436-78-4 (calcium dependent protein kinas C)
141588-27-4 (cGMP-dependent protein kinase)
142008-29-5 (cAMP-dependent protein kinase)
191808-15-8 (phosphoinositide dependent protein kinase 1)
377752-08-4 (ribosomal protein S6 kinase 2)
389133-24-8 (ribosomal S6 kinase 3)
90698-26-3 (ribosomal protein S6 kinase 1)

2 Source Organism

<1> *Paramecium primaurelia* [1]
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<53> *Bos taurus* [109, 110]
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<178> *AKT8 murine leukemia virus* [340]
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<290> *Mus musculus* [504]

3 Reaction and Specificity

Catalyzed reaction

ATP + a protein = ADP + a phosphoprotein

Reaction type

phospho group transfer

Natural substrates and products

S ATP + S6 protein of the 40s ribosomal subunit <165> (<165>, the mitogen-activated protein kinase plays a central role in the control of mRNA translation. It physiologically phosphorylates the S6 protein of the 40s ribosomal subunit in response to mitogenic stimuli and is a downstream component of the rapamycin-sensitive pathway, which includes the 12-kDa FK506 binding protein and includes rapamycin and the 12-kDa FK506 binding protein target 1 [311]) (Reversibility: ? <165> [311]) [311]

P ADP + phosphorylated S6 protein of the 40s ribosomal subunit

S ATP + protein <44, 48> (<44>, the enzyme mediates agonist-dependent phosphorylation of the β2-adrenergic and related G protein-coupled receptors [98]; <44>, specifically phosphorylates the agonist-occupied forms of the β 2-adrenergic receptor and related G protein-coupled receptors [101]; <48>, specifically phosphorylates the agonist-occupied form of the β-adrenergic and related G protein-coupled receptors [106]) (Reversibility: ? <44, 48> [98, 101, 106]) [98, 101, 106]

P ATP + phosphoprotein

S ATP + protein kinase Cζ <98> (<98>, phosphorylation and activation of protein kinase Cζ [179]) (Reversibility: ? <98> [179]) [179]

P ADP + phosphorylated protein kinase Czeta

S ATP + rhodopsin <53, 76, 86, 96> (<53>, light-dependent deactivation of rhodopsin involves receptor phosphorylation that is mediated by the highly specific protein kinases rhodopsin kinase [109]; <76>, null mutations in the rhodopsin kinase gene are a cause of Oguchi disease and extend the known genetic heterogeneity in congenital stationary night blindness [147]; <96>, enzyme is required for normal rhodopsin deactivation. Abnormal photoresponses and light-induced apoptosis in rods lacking rhodopsin kinase [177]) (Reversibility: ? <53, 76, 86, 96> [109, 146, 147, 148, 177]) [109, 146, 147, 148, 177]

P ADP + phosphorylated rhodopsin

S Additional information <107, 109, 110, 111, 113, 115, 122, 124, 125, 135, 137, 145> (<107>, induction of enzymatically active Sgk functions as a key cell survival component in response to different environmental stress stimuli [181]; <109>, protein kinase C β controls nuclear factor κB activation in B cells through selective regulation of the κB kinase α [183]; <110>, protein kinase Cδ controls self-antigen-induced B-cell tolerance [184]; <111>, K^+-channel activation by all three isoforms of serum-dependent and glucocorticoid-dependent protein kinase SGK [185]; <115>, kinase plays a role in human visual signaling [189]; <110>, key regulatory role in a variety of cellular functions, including apoptosis, as well as cell growth and differentiation [191]; <113>, AKT1 gene is not a major contributor to susceptibility to type II diabetes mellitus in Ashkenazi Jews [192]; <107>, induction of sgk by aldosterone is detected in kidney cortex and medulla, whereas the papilla express a constitutively high level of the

kinase [194]; <107>, enzyme plays an important role in the early phase of aldosterone-stimulated Na^+ transport [195]; <107>, transcriptional target of p53 in mammary epithelial cells, hormone-regulated protein kinase gene with a functionally defined p53 promoter recognition element [196]; <109>, overproduction of protein kinase C causes disordered growth control in rat fibroblasts, activation of PKC may be of central importance in the process of multistage carcinogenesis [204]; <110>, PKC δ is involved in fundamental cellular functions regulated by diacylglycerols and mimicked by phorbol esters [211]; <111>, the enzyme acts in concert with Akt to propagate the effects of PI3K activation within the nucleus and to mediate the biological outputs of PI3K signaling, including cell survival and cell cycle progression [213]; <111>, deranged transcriptional regulation of cell-volume-sensitive kinase hSGK in diabetic nephropathy [214]; <111>, transcript levels are strongly altered during anisotonic and isotonic cell volume changes [218]; <122>, PKC ζ action is involved in growth and differentiation of the collecting duct [241]; <124>, the enzyme is required to repress entry into the conidiation program [242]; <125>, NPH1 is an autophosphorylating flavoprotein photoreceptor mediating phototropic responses in higher plants [245]; <135>, the enzyme is a phorbol ester receptor [264]; <137>, PKC ζ exhibits a constitutive kinase [268]; <145>, PKC δIII may show a dominant negative effect against PKC δI [286]) [181, 183, 184, 185, 189, 192, 194, 195, 196, 204, 211, 213, 214, 241, 242, 245, 264, 268, 286]

P ?

S Additional information <153, 158, 163, 164, 166, 167, 173, 178, 180, 181, 182, 185, 198, 203> (<153,163>, enzyme is required for cell growth [296]; <158>, protein kinase C-ε increases growth and cause malignant transformation when overexpressed in NIH3T3 cells the catalytic domain of PKC-ε, in reciprocal PKC-δ and PKC-ε chimeras, is responsible for conferring tumorgenicity to NIH3T3 cells, whereas both regulatory and catalytic domains of PKC-ε contribute to in vitro transformation [301]; <164>, plays a central role in the control of proliferation and differentiation of a wide range of cell types by mediating the signal transduction response to hormones and growth factors [308]; <166>, kinase plays a part in regulating events associated with fertilization [315]; <167>, DBF2 mRNA is expressed under cell-cycle control at or near START [316]; <182>, the DBF20 mRNA is expressed at a low level and not under cell-cycle control [316]; <167>, DBF2 is likely to encode a protein kinase that may function in initiation of DNA synthesis and also in late nuclear division [317]; <173>, PKC1-depleted cells arrested growth with small buds. PKC_1 may regulate a previously unrecognized checkpoint in the cell cycle [333]; <178>, enzyme may form a functional link between tyrosine and serine-threonine phosphorylation pathways [340]; <180>, AKT2 may contribute to the pathogenesis of ovarian carcinomas [342]; <181>, enzyme is involved in fertilization [344]; <185>, Gprk2 is required for egg morphogenesis [349]; <203>, enzyme may function in the adaptation of plant cells to cold or high-salt conditions [378]; <203>, atpk1 is involved in

the control of plant growth and development [380]) [296, 301, 308, 315, 316, 317, 333, 340, 342, 344, 349, 370, 378, 380]

P ?

S Additional information <203, 216, 242, 243, 244, 245, 248, 254, 267, 270, 285, 290> (<216>, mutations in the ribosomal S6 kinase (Rsk-2) gene are associated with Coffin-Lowry syndrome, an X-linked disorder characterized by facial dysmorphism, digit abnormalities and severe psychomotor retardation [396,397,398]; <216> inherited defects in insulin-stimulated activation of muscle glycogen synthesis in patients with insulin-resistant NIDDM may be located further upstream of ISPK-1 in the insulin action cascade [399]; <242>, enzyme may play a role in signal transduction and growth regulatory pathways unique to hematopoietic cells [438]; <243>, constitutive enzyme [268]; <244>, PKC-δ desensitizes the Pkc1-mediated pathway by regulating an aspect of G protein function [440]; <245>, SGK is a component of the phosphoinositide 3 (PI 3)-kinase signaling pathway [442]; <245>, the enzyme is transcriptionally regulated by serum and glucocorticoids in mammary epithelial cells, hormone-regulated protein kinase gene with a functionally defined p53 promoter recognition element [196]; <245>, enzyme is induced during ovarian cell differentiation [442]; <245>, induction of sgk gene may be associated with a series of axonal regenerations after brain injury, and in addition, the sgk gene may also play important roles in the development of particular groups of neurons in the postnatal brain [444]; <245>, the enzyme is highly regulated at the transcriptional level by glucocorticoid hormones [445]; <248>, T-PK may have specialized functions in different areas of central nervous system. Alterations of this complex expression pattern can be responsible for the mental status impairment observed in myotonic dystrophy patients [449]; <248>, enzyme may have a role in the development of mental symptoms in severe cases of myotonic dystrophy [451]; <248>, decreased expression of myotonin-protein kinase messenger RNA and protein in adult form of myotonic dystrophy [452]; <254>, in normal rat kidney cells, predominant phosphorylation of a 30000 Da protein at serine residues, constitutive low level expression in normal tissues, elevated expression levels in selected tumor cell lines, a role of PKC μ in signal transduction pathways related to growth control [462]; <203>, may function in the adaptation of plant cells to cold or high-salt conditions [378]; <267>, Akt2 expression is activated during cellular differentiation and may function in the signaling pathways of some adult tissues [480]; <270>, enzyme mainly involved in homologous desensitization of the TSH receptor [484]; <285>, ribosomal S6-kinase RSK4 is commonly deleted in patients with complex X-linked mental retardation, RSK4 plays a role in normal neuronal development. RSK4 is completely deleted in eight patients with the contiguous gene syndrome including MRX, partially deleted in a patient with DFN3 and present in patients with an Xq21 deletion and normal intellectual abilities [500]; <290>, enzyme is important for cell growth [504]) [268, 378, 396, 397, 398, 399, 438, 440, 442, 444, 445, 449, 451, 452, 462, 480, 484, 500, 504]

P ?

S Additional information <2, 7, 23, 30, 34, 38, 44, 47, 49, 58, 70, 73> (<44>, role for β ARK in modulating some receptor-mediated immune functions [99]; <7>, amino acid sequence at the ATP-binding site of cGMP-dependent protein kinase [7]; <23>, the enzyme positively regulates the progression of yeast cells through the G1 phase of the cell cycle [54]; <23>, the enzyme is part of a growth control pathway which is at least partially redundant with the cAMP pathway [56]; <30,73>, enzyme plays a crucial role in the relaxation of vascular smooth muscle by lowering the intracellular level of calcium [77]; <34>, the enzyme plays a central role in the control of mammalian sperm capacitation and motility [84]; <38>, enzyme is important in mediating rapid agonist-specific desensitization [90]; <47,49>, general role in the desensitization of synaptic receptors [104]; <58>, enzyme plays an essential role during differentiation and fruit morphogenesis in Dictyostelium discoideum [116]; <70>, the enzyme is thought to be involved in the regulation of intestinal ion transport and fluid secretion [134]; <70>, plays a pivotal role in the regulation of intestinal fluid balance in man [135]; <73>, enzyme is involved in inhibition of platelet aggregation, relaxation of smooth muscle cells, and control of cardiocyte contractility. Pathophysiological implication of the type I cGK in cardiovascular diseases, including hypertension and atherosclerosis [140]) [2, 7, 54, 56, 77, 84, 90, 99, 104, 116, 134, 135, 140]

P ?

Substrates and products

S ATP + PKC-α-derived peptide <137> (<137>, in the presence of the classical PKC activators phosphatidylserine/diacylglycerol, PKC α phosphorylates a PKC-α pseudosubstrate-derived peptide, an epidermal-growth-factor-receptor-derived peptide, histone III-S and myelin basic protein to an equal extent, whilst PKC ζ phosphorylates only the PKC-α-derived peptide [268]) (Reversibility: ? <137> [268]) [268]

P ADP + phosphorylated PKC-α-derived peptide

S ATP + S6 protein of the 40s ribosomal subunit <165> (<165>, the mitogen-activated protein kinase plays a central role in the control of mRNA translation. It physiologically phosphorylates the S6 protein of the 40s ribosomal subunit in response to mitogenic stimuli and is a downstream component of the rapamycin-sensitive pathway, which includes the 12-kDa FK506 binding protein and includes rapamycin and the 12-kDa FK506 binding protein target 1 [311]) (Reversibility: ? <165> [311]) [311]

P ADP + phosphorylated S6 protein of the 40s ribosomal subunit

S ATP + activated form of G protein-coupled receptors <181> [346]

P ADP + phosphorylated G protein-coupled receptors

S ATP + β2-adrenergic receptor <205, 206> (<205>, phosphorylation in an agonist-dependent manner, phosphorylates the C-terminal tail regions of both receptor proteins [382]) (Reversibility: ? <205,206> [382,384]) [382, 384]

P ADP + phosphorylated β2-adrenergic receptor

S ATP + histone H1 <113, 116> (<116>, PKD2 activated by phorbol esters efficiently phosphorylate the exogenous substrate histone H1 [190]) (Reversibility: ? <113,116> [190,224]) [190, 224]
P ADP + phosphorylated histone H1
S ATP + histone IIIS <275> (<275>, poor substrate [489]) (Reversibility: ? <275> [489]) [489]
P ADP + phosphorylated histone IIIS
S ATP + myelin basic protein <202, 204> (Reversibility: ? <,202,204> [377,381]) [377, 381]
P ADP + phosphorylated myelin basic protein
S ATP + plant ribosomal proteins <203> (<203>, two plant ribosomal proteins of 14000 Da and 16000 Da can be phosphorylated by the Atpk1 protein kinase [379]) (Reversibility: ? <203> [379]) [379]
P ADP + phosphorylated plant ribosomal proteins
S ATP + protein <125> (<125>, autophosphorylation [245]; <125>, blue light-dependent autophosphorylating [244]) (Reversibility: ? <125> [244, 245]) [244, 245]
P ADP + phosphoprotein
S ATP + protein <205> (<205>, major autophosphorylation sites are Ser484 and Thr485 [382]) (Reversibility: ? <205> [382]) [382]
P ADP + phosphoprotein
S ATP + protein <238, 254, 258, 259, 268, 269, 273> (<238, 254, 258, 259, 268, 269, 273>, autophosphorylation [433, 462, 469, 481, 482, 487]; <269>, Ser916 is an in vivo autophosphorylation site [482]) (Reversibility: ? <238, 254, 258, 259, 268, 269, 273> [433, 462, 469, 481, 482, 487]) [433, 462, 469, 481, 482, 487]
P ADP + phosphoprotein
S ATP + protein <7, 44, 48, 53, 97> (<7, 53, 97>, autophosphorylation [8,110,178]; <44>, specifically phosphorylates the agonist-occupied forms of the β2-adrenergic receptor and related G protein-coupled receptors [101]; <44>, the enzyme mediates agonist-dependent phosphorylation of the β2-adrenergic and related G protein-coupled receptors [98]; <48>, specifically phosphorylates the agonist-occupied form of the β-adrenergic and related G protein-coupled receptors [106]) (Reversibility: ? <7, 44, 48, 53, 97> [8, 98, 101, 106, 110, 178]) [8, 98, 101, 106, 110, 178]
P ADP + phosphoprotein
S ATP + protein kinase Cζ <98> (<98>, phosphorylation and activation of protein kinase Cζ [179]) (Reversibility: ? <98> [179]) [179]
P ADP + phosphorylated protein kinase Cζ
S ATP + rhodopsin <181, 205, 206> (<181>, reaction only with GRK4α isoform, no reaction with GRK4β, GRK4γ, GRK4δ [344]; <205>, GRK5 phosphorylates rhodopsin in a light-dependent manner, phosphorylates the C-terminal tail region [382]) (Reversibility: ? <181,205,206> [344,382,384]) [344, 382, 384]
P ADP + phosphorylated rhodopsin
S ATP + rhodopsin <53, 76, 86, 96> (<53>, light-dependent deactivation of rhodopsin involves receptor phosphorylation that is mediated by the

highly specific protein kinases rhodopsin kinase [109]) (Reversibility: ? <53, 76, 86, 96> [109, 146, 147, 148, 177]) [109, 146, 147, 148, 177]
P ADP + phosphorylated rhodopsin
S ATP + ribosomal protein S6-(229-239) peptide analogue <272> (Reversibility: ? <272> [486]) [486]
P ADP + phosphorylated ribosomal protein S6-(229-239) peptide analogue
S Additional information <170, 204, 206, 210> (<170>, phorbol ester receptor/protein kinase [326]; <204>, preferably phosphorylates the Saccharomyces cerevisiae Pkc1p pseudosubstrate peptide and myelin basic protein, but not histones, protamine or dephosphorylated casein [381]; <206>, GRK6, but not other GRKs tested, incorporated tritium after incubation with [^{3}H]palmitate in Sf9 and in COS-7 cells overexpressing the kinase [383]; <210>, interaction between RAC-PK and protein kinase C [390]) [326, 381, 383, 390]
P ?

Inhibitors

1-(5-isoquinolinesulfonyl)-2-methylpiperazine <110> [191]
1-oleoyl-2-acetylglycerol <269> (<269>, inhibits phorbol ester binding [483]) [483]
Ro 31-8220 <114> [227]
calmodulin <181> (<181>, reaction of isoenzyme GRK4α with rhodopsin, IC50: 80 nM [344]) [344]
staurosporine <8, 114, 193, 194> [14, 227, 364]
Additional information <110> (<110>, insensitive to caspase-3 [191]) [191]
Additional information <243> (<243>, insensitive to PKC inhibitors known to interfere either with the regulatory or the catalytic domain [268]) [268]
Additional information <8> (<8>, modification and concomitant inactivation of the catalytic subunit of bovine heart cAMP-dependent protein kinase with affinity analogs of peptide substrates potentially capable of undergoing disulfide interchange with enzyme-bound sulfhydryl groups [12]) [12]

Cofactors/prosthetic groups

3-phosphoinositide <4, 98> (<4,98>, enzyme is dependent on [4,179]) [4, 179]
8-bromo-cAMP <66> (<66>, 50% activation at 0.00062 mM [130]) [130]
8-bromo-cGMP <66> (<66>, 50% activation at 0.00004 mM [130]) [130]
FMN <125> (<125>, apoprotein noncovalently binds FMN to form the holoprotein nph1 [244]) [244]
cAMP <1, 8, 9, 11, 12, 14, 15, 27, 34, 37, 40, 41, 52, 58, 61, 62, 66> (<1, 8, 9, 11, 12, 27, 37, 40, 41, 58, 61, 62>, dependent on [1, 3, 12, 13, 14, 17, 24, 25, 27, 28, 29, 30, 31, 32, 67, 68, 69, 89, 93, 116, 117, 118, 122, 123, 124]; <66>, 50% activation at 0.0117 mM, activation is not cooperative [130]) [1, 3, 12, 13, 14, 17, 24, 25, 27-32, 67-69, 84, 89, 93, 108, 116-118, 122-124, 130]
cGMP <6, 7, 30, 36, 57, 66, 70, 73, 84, 88, 97> (<6, 7, 30, 36, 57, 66, 70, 73, 84, 88, 97>, dependent on [6, 7, 8, 9, 10, 11, 67, 77, 78, 88, 115, 133, 134, 135, 140,

161, 166, 178]; <66>, cGMP, 0.010 mM, stimulated histone H2B phosphorylation by the DG1 protein kinase 20-fold [130]; <66>, 50% activation at 0.00019 mM, cooperative activation [130]) [6, 7, 8, 9, 10, 11, 67, 77, 78, 88, 115, 130, 133, 134, 135, 140, 161, 166, 178]
cIMP <66> (<66>, 50% activation at 0.0053 mM [130]) [130]
flavin <125> (<125>, LOV1 and LOV2 may be flavin-binding domains that regulate kinase activity in response to blue light-induced redox changes [246]; <125>, flavoprotein [246]) [245, 246]

Activating compounds

AMP <166> (<166>, dependent on AMP [315]) [315]
arachidonic acid <137> (<137>, alone or a combination of γ-linolenic acid and phosphatidylserine slightly enhances PKC ζ activity [268]) [268]
arachidonic acid <243> (<243>, slightly enhances PKC ζ activity [268]) [268]
cardiolipin <272> (<272>, activates [486]) [486]
diacylglycerol <137, 140, 145> (<140> activates [272]; <137>, plus phosphatidylserine, activates [268]; <145>, activity is dependent on [290]) [268, 272, 290]
diacylglycerol <146> (<146>, activity is dependent on [290]; <147>, independent of the presence of Ca^{2+} or diacylglycerol, when assayed with calf thymus H1 histone as a phosphate acceptor protein [292]) [290]
diacylglycerol <244> (<244>, dependent upon phosphatidylserine or diacylglycerol for maximal activation [441]) [441]
γ-linolenic acid <243> (<243>, a combination of γ-linolenic acid and phosphatidylserine slightly enhances PKC zeta activity [268]) [268]
gastrin <116> (<116>, physiological activator of PKD2 in human AGS-B cells stably transfected with the CCK(B)/gastrin receptor [190]) [190]
insulin <113> (<113>, activated endogenous protein kinase B $\alpha_1$2-fold in L6 myotubes, while after transfection into 293 cells PKBα is activated 20- and 50-fold in response to insulin and IGF-1 respectively. In both cells, the activation of PKBα is accompanied by its phosphorylation at Thr308 and Ser473 [221]) [221]
neurabin <165> (<165>, by way of its PDZ domain, the neuronal-specific neurabin may target p70(S6k) to nerve terminals [311]) [311]
pervanadate <113> (<113>, activation of Akt is associated with tyrosine phosphorylation of Akt [187]) [187]
phorbol dibutyrate <140> (<140>, activates [272]) [272]
phorbol esters <174> (<174>, bind to and stimulate the kinase activity of PKC-L [336]) [336]
phorbol esters <234> (<234>, stimulate [429]) [429]
phosphatidylserine <137> (<137>, plus diacylglycerol, activates [268]) [268]
phosphatidylserine <243> (<243>, a combination of γ-linolenic acid and phosphatidylserine slightly enhances PKC zeta activity [268]) [268]
phosphatidylserine <244, 260, 261> (<244>, dependent upon phosphatidylserine or diacylglycerol for maximal activation [441]; <260>, stimulates [471]; <260,261>, PKC Apl I requires much less phosphatidylserine for activation than does purified PKC Apl II [471,474]) [441, 471, 474]

phospholipid <110, 145> (<110>, strict dependence on the presence of phospholipids, [212]; <145>, activity is dependent on [290]) [212, 290]
phospholipid <146, 147> (<146>, activity is dependent on [290]; <147>, significantly dependent on phospholipid when assayed with calf thymus H1 histone as a phosphate acceptor protein [292]) [290]
phospholipid <275, 278> (<275>, dependent on [489]; <278>, stimulates [429]) [429, 489]
serum <113> (<113>, activation of Akt is associated with tyrosine phosphorylation of Akt [187]) [187]
Additional information <111, 113> (<111>, activation of serum-regulated and glucocorticoid-regulated protein kinase by agonists that activate phosphatidylinositide 3-kinase is mediated by 3-phosphoinositide-dependent protein kinase-1 and PDK2 [215]; <111>, activation of SGK by IGF-1 or hydrogen peroxide is initiated by a PtdIns(3,4,5)P3-dependent activation of PDK2, which phosphorylates Ser422. This is followed by the PtdIns(3,4,5)P3-independent phosphorylation at Thr256 that activates SGK, and is catalysed by PDK1 [216]; <113>, PKBα becomes phosphorylated and activated in insulin/IGF$^-$1-stimulated cells by an upstream kinase(s) [221]) [215, 216, 221]
Additional information <243, 245> (<243>, cannot be activated by phorbol ester treatment of NIH 3T3 cells or insect cells, overexpressing the respective PKC isoenzyme [268]; <245>, transcriptionally regulated by serum and glucocorticoids in mammary epithelial cells [442]) [268, 442]
Additional information <7> (<7>, aminoterminal dimerization site of cGMP-dependent protein kinase and the autophosphorylation site, present in this part, control not only the activation of the enzyme but also the cooperative binding characteristics of the intact enzyme [8]) [8]

Metals, ions

Ca^{2+} <109> (<109>, Ca^{2+}-mediated interactions between the two domains could contribute to enzyme activation as well as to the creation of a positively charged phosphatidylserine-binding site [198]; <110>, no activation [212]; <137>, activity is independent of Ca^{2+} [268]) [198]
Ca^{2+} <260> (<260>, enzyme is dependent on Ca^{2+} [471]; <260>, activates [472]) [471, 472]
Mg^{2+} <66> (<66>, maximal activation at 40-50 mM [130]) [130]
Additional information <202> (<202>, presence of only one cysteine-rich, zinc finger-like domain, absence of an apparent Ca(2+)-binding region [377]) [377]

K_m-Value (mM)

0.0036 <272> (S6-(229-239) peptide, <272>, enzyme activated by cardiolipin [486]) [486]

4 Enzyme Structure

Molecular weight

Additional information <8> (<8>, amino acid sequence of the catalytic subunit [15]) [15]

Subunits

? <116> (<116>, x * 105000, SDS-PAGE [190]) [190]

? <147, 165, 202, 203> (<203> x * 52554, calculation from nucleotide sequence [380]; <165>, x * 56160 [312]; <165>, x * 59109 [313]; <147>, x * 64000, SDS-PAGE [292]; <202>, x * 65000 [377]) [380, 313, 312, 292, 377]

? <238, 245, 248, 258, 272, 278> (<245>, x * 49000 [445]; <248>, x * 70000 [450]; <238>, x * 79000, SDS-PAGE [433]; <258>, x * 103925, calculation from nucleotide sequence [470]; <272>, x * 116000 [486]; <258>, x * 120000, SDS-PAGE [470]; <278>, x * 126000 [429]) [429, 433, 445, 450, 470, 486]

? <7, 30> (<7>, x * 76331 [10]; <30>, x * 77803, calculation from nucleotide sequence [78]) [10, 78]

Additional information <171> (<171> p70 S6 kinase α I with a calculated MW of 58946 Da consists of 525 amino acids, of which the last 502 residues are identical in sequence to the entire polypeptides encoded by the p70 S6 kinase α II with a calculated MW of 56153 Da. Both p70 S6 kinase polypeptides predicted by these cDNAs are present in p70 S6 kinase purified from rat liver, and each is thus expressed in vivo. The slightly longer α I polypeptide exhibits anomalously slow mobility on SDS-PAGE, migrating at an apparent MW of 90000 Da probably because of the presence of six consecutive Arg residues immediately following the initiator methionine [327]) [327]

Additional information <8, 14, 37, 58, 61> (<8>, MW of the catalytic subunit determined by amino acid sequence is 40580 Da [16]; <14>, three different genes encode the catalytic subunits of the cAMP-dependent protein kinase [30]; <37>, MW of the catalytic subunit C is 39000-41000 Da [89]; <58>, PkaC is a catalytic subunit of the Dictyostelium discoideum cAPK [116]; <61>, the product of pka1 is a catalytic subunit of protein kinase A [122]) [16, 30, 89, 116, 122]

Posttranslational modification

lipoprotein <206> (<206>, palmitoylation of GRK6 appears essential for membrane association [383]) [383]

phosphoprotein <109, 110, 113, 114, 116> (<113>, in SKOV3 ovarian carcinoma cells that exhibit high basal levels of Akt activity, Akt is tyrosine-phosphorylated in the basal state, and this phosphorylation is further enhanced by both pervanadate and insulin-like growth factor-1, Tyr474 is the site of tyrosine phosphorylation [187]; <116>, phorbol 12,13-dibutyrate in the presence of dioleoylphosphatidylserine stimulates the autophosphorylation of PKD2 in a synergistic fashion. Phorbol esters also stimulate autophosphorylation of PKD2 in intact cells, C-terminal Ser876 is an in vivo phosphorylation site within PKD2 that is correlated with the activation status of the kinase [190];

<109>, protein kinase C is processed by three phosphorylations. Firstly, trans-phosphorylation on the activation loop T500 renders it catalytically competent to autophosphorylate. Secondly, a subsequent autophosphorylation on the carboxyl terminus T641 maintains catalytic competence. Thirdly, a second autophosphorylation on the carboxyl terminus S660 regulates the enzyme's subcellular localization [199]; <109>, phosphorylation of Thr642 is an early event in the processing of newly synthesized protein kinase C β 1 and is essential for its activation [200]; <109>, processing by protein kinase C cannot occur until the enzyme is first phosphorylated by a protein kinase C kinase [201]; <109>, COOH-terminal autophosphorylation sites are critical for enzyme function and possibly subcellular localization in COS cells [202]; <110>, activation loop phosphorylation of PKCδ in response to serum stimulation of cells is PI 3-kinase-dependent and is enhanced by PDK1 coexpression [209]; <114>, two splice variants of protein kinase B γ have different regulatory capacity depending on the presence or absence of the regulatory phosphorylation site Ser472 in the carboxyl-terminal hydrophobic domain [225]; <114>, Akt3 is phosphorylated in response to insulin [226]; <114>, Akt-3 also possess a C-terminal 'tail' that contains a phosphorylation site Ser472 thought to be involved in the activation of Akt kinases. In addition to phosphorylation of Ser472, phosphorylation of Thr305 also appears to contribute to the activation of Akt-3 [227]; <114>, regulatory phosphorylation sites in the activation loop and in the C-terminal hydrophobic domain, Thr305 and Ser472, phosphorylation of both sites is required for full activity [228]) [187, 190, 199, 200, 201, 202, 209, 225, 226, 227, 228]

phosphoprotein <114, 286> (<114,286>, two splice variants of protein kinase B γ have different regulatory capacity depending on the presence or absence of the regulatory phosphorylation site Ser472 in the carboxyl-terminal hydrophobic domain, activation of PKB γ 1 requires phosphorylation at a single regulatory site Thr305 [225]; <114,286>, regulatory phosphorylation sites in the activation loop and in the C-terminal hydrophobic domain, Thr305 and Ser472 [225]) [225]

phosphoprotein <205> (<205>, major autophosphorylation sites are Ser484 and Thr485 [382]) [382]

phosphoprotein <7, 8> (<7>, autophosphorylation [8,9]; <8>, phosphate groups at Thr196 and Ser337 [16]) [8, 9, 16]

Additional information <109> (<109>, two types of complementary DNA clones for rat brain protein kinase C, these clones encode 671 and 673 amino acid sequences, which differ from each other only in the carboxyl-terminal regions of approximately 50 amino acid residues. This difference seems to result from alternative splicing [207]) [207]

Additional information <34> (<34>, unmyristylated Cα_2 may be essential for fertility in the male [85]) [85]

5 Isolation/Preparation/Mutation/Application

Source/tissue

3T3 cell <164> [310]
AGS <116> (<116>, AGS-B cell [190]) [190]
HL-60 cell <116> [190]
SKOV-3 cell <113> [187]
aorta <233> [428]
blood platelet <242> [437]
brain <109, 110, 111, 113, 135, 139, 140, 145> (<139>, in adult brain, the relative activities of α-, β I-, β II-, and γ-subspecies are roughly 16%, 8%, 55%, and 21% [271]) [191, 206, 207, 208, 211, 216, 224, 264, 270, 271, 290]
brain <146, 147, 148, 152, 181, 202, 205, 206> (<205>, very weak activity [382]) [281, 290, 292, 295, 345, 377, 382, 384]
brain <233, 241, 242, 245, 248, 268, 273, 285> (<245>, the cells which strongly express the sgk gene are in the deep layers of the cortex and in the corpus callosum. It is likely that the sgk transcript is expressed by oligodendrocytes after brain injury. Neurons in layers I and II of the cortex, lateroposterior and laterodorsal thalamic nucleus, and ventral posterolateral and posteromedial thalamic nucleus strongly express sgk mRNA at postnatal day 1 and day 7, but these neurons show no expression in fetal or adult brain. Induction of sgk gene may be associated with a series of axonal regenerations after brain injury, and in addition, the sgk gene may also play important roles in the development of particular groups of neurons in the postnatal brain [444]; <248>, different expression of the myotonin protein kinase gene in discrete areas of brain [449]) [428, 436, 437, 444, 449, 451, 481, 487, 500]
brain <38, 47, 49, 88> (<47,49>, synapses [104]; <47>, β-ARK mRNA is expressed intensely in the cerebellar granule cell layer and moderately in the hippocampal pyramidal cells and dentate granule cells. The neocortex and piriform cortex express it moderately to weakly, whereas the thalamus and hypothalamus express it weakly to faintly. No significant expression of the mRNA is detected in the caudate-putamen. Weak expression of β-ARK mRNA in several nuclei of the brainstem and in the spinal gray matter [105]) [90, 104, 105, 166]
cardiac muscle <8> [16]
cell culture <107, 111, 113> (<107>, NMuMG epithelial cell line [196]; <111>, hepatoma cell line [218]; <113>, cell lines MCF-7 and WI38 [223]; <113>, SKOV3 ovarian carcinoma cell [187]) [187, 196, 218, 223]
cell culture <160, 174, 180, 181, 202> (<160>, PR-17 cells and wild-type HL-60 cells [304]; <164>, Swiss 3T3 fibroblasts [310]; <174>, epidermoid carcinoma line A431 [336]; <164>, fibrosarcoma cell line [309]; <180>, ovarian carcinoma cell lines [342]; <180>, cell lines MCF-7 and WI38 [343]; <181>, spermatogonia cell line GC-1 spg [344]; <202>, insulin-secreting cell line RINm5F [377]) [304, 309, 310, 336, 342, 343, 344, 377]
cell culture <216, 241, 245, 268> (<216>, HeLa cells [400]; <241>, several hemopoietic tumor lines [436]; <245>, Con8.hd6 rat mammary tumor cell

line [445]; <268>, undifferentiated mouse embryonal carcinoma cell line P19, NIH 3T3 cells [481]) [400, 436, 445, 481]
cell culture <13, 45, 52> (<45>, ovary cell line [26]; <52>, myoblast L6 cell line [108]) [26, 108]
collecting duct <107> [195]
colon <107> [194]
colon <270> [484]
embryo <37, 98> [89, 179]
embryo <245> (<245>, embryo kidney 293 cells [442]) [442]
erythroleukemia cell <283> [498]
fibroblast <109, 113> [204, 224]
fibroblast <70> (<70>, in normal diploid fibroblasts, the gene is constitutively expressed during cell-cycle and population doubling levels [133]) [133]
fibrosarcoma cell line <164> [309]
frontal cortex <243> [439]
germ <181> [344]
heart <113> [224]
heart <233> [428]
heart <174, 205, 206> (<205>, high activity [382]) [335, 336, 382, 384]
heart <6, 8, 89> (<6>, expressed at a much higher level in newborn than in adult [6]; <89>, enhanced expression of β-adrenergic receptor kinase 1 in the hearts of cardiomyopathic Syrian hamsters, BIO53.58 [167]) [6, 12, 167]
hematopoietic cell <110, 116> (<116>, hematopoietic stem cell and hemopoietic progenitor cells [229]) [212, 229]
hematopoietic cell <242> (<242>, enzyme is predominantly expressed in [438]) [438]
hepatoma cell <165> [314]
hippocampus <258> [470]
intestine <88> (<88>, intestinal mucosa [166]) [166]
kidney <88> [166]
kidney <233, 254, 268, 270, 285> [428, 462, 481, 484, 500]
kidney <107, 110, 111, 122> (<122>, cortex [241]; <122>, low expression in vascular elements and high expression in tubule epithelium, highly expressed in proximal tubule, thick limb, and collecting duct [241]) [191, 194, 216, 241]
kidney <205> (<205>, very weak activity [382]) [382]
larva <37> [89]
larva <190> (<190>, abundant at the earliest larval stage, but their relative concentrations decrease coordinately in late larvae [361]) [361]
leukocyte <141> [277]
leukocyte <44, 59> (<44,59>, peripheral blood leukocytes [99,120]) [99, 120]
liver <233, 272> [428, 486]
liver <111, 114> (<114>, not highly expressed [227]) [216, 227]
liver <165, 171, 205, 206> (<205>, very weak activity [382]) [312, 327, 382, 384]
lung <113> [224]
lung <7> [9, 10]

lung <170, 174, 202, 205, 206> (<205>, high activity [382]) [326, 335, 336, 377, 382, 384]
lung <233, 241, 242, 245, 270> (<245>, high activity [445]) [428, 436, 437, 445, 484]
mammary epithelium <245> [196]
mature ovarian follicle <245> [443]
megakaryoblast <242> [437]
myeloid cell <110> (<110>, ABPL-3 myeloid tumor [212]) [212]
nervous system <260, 261> [472]
ovary <149, 150> [293]
ovary <110> (<110>, highly expressed [191]) [191]
ovary <245, 268> (<245>, high activity [445]) [445, 481]
pancreas <111> [216]
pancreas <206> [384]
pancreatic islet <202> [377]
pineal gland <76> [148]
placenta <206> [384]
placenta <216> [399]
placenta <30> [78]
retina <115> [189]
retina <44> [98]
retina <205> (<205>, high activity [382]) [382]
retinal cone <115> [189]
sensory cell <260, 261> [473]
skeletal muscle <206> [384]
skeletal muscle <114> (<114>, not highly expressed [227]) [227]
skeletal muscle <233, 242, 255> (<233>, predominantly expressed in [428]) [428, 437, 463]
skin <170, 174> [326, 335, 336]
small intestine <70> [134]
small intestine <233> [428]
sperm <34> [84, 85]
sperm <181> (<181>, GRK4γ is the only detectable isoform in human sperm [344]) [344]
spermatozoon <166, 181> (<166>, transcripts encoding CAPL-B, an apparent member of the cyclic-nucleotide-regulated kinase subfamily in Aplysia californica, are found exclusively in the ovotestis and are concentrated in meiotic and postmeiotic spermatogenic cells. The CAPL-B polypeptide is present in mature spermatozoa [315]) [315, 344]
stomach <233> [428]
testis <98> [179]
testis <241, 268> [436, 481]
testis <40> [94]
testis <110> (<110>, highly expressed [191]) [191]
testis <181, 205, 210, 211> (<205>, very weak activity [382]) [344, 382, 390]
thymocyte <110> [191]
thymus <233, 245, 290> (<245>, high activity [445]) [428, 445, 504]

thyroid gland <270> [484]
tongue epithelium <205> [382]
trachea <7> (<7>, trachea smooth muscle [11]) [11]
uterus <233> [428]
Additional information <111, 114> (<111>, SGK3 is expressed in all tissues examined, but SGK2 mRNA is only present at significant levels in liver, kidney and pancreas and, at lower levels, in the brain [216]; <114>, expressed widely [227]) [216, 227]
Additional information <12, 37> (<12>, C α mRNA is widespread and highly expressed in brain, heart, adrenal gland, testis, lung, kidney, spleen and liver, whereas the C β mRNA is unevenly expressed in the brain and adrenal gland and in much lesser amounts in other tissues [27]; <37>, expressed at a low level in cytosolic and particulate compartments during embryogenesis. As the nematodes progress from late embryonic stages to the newly hatched, first larval stage, C subunit content increases 15fold. High levels of C subunits are observed in several subsequent larval and adult stages of development [89]) [27, 89]
Additional information <205> (<205>, most abundantly in lung, heart, retina, and lingual epithelium, but expressed very little in brain, liver, kidney, or testis [382]) [382]

Localization

cytoplasm <145> [286]
cytoplasm <272> [486]
cytoskeleton <190> (<190>, associated with [361]) [361]
cytosol <37> [89]
cytosol <145> (<145>, stimulation by phorbol ester causes weak translocation of δIII$^-$GFP from the cytosol to the plasma membrane [286]) [286]
membrane <88> [166]
membrane <164, 190, 205> (<190>, associated with [361]; <205>, GRK5 protein does not undergo agonist-dependent translocation from cytosol to membranes as do β-adrenergic receptor kinase and rhodopsin kinase, but rather appears to associate with membranes constitutively [382]) [309, 361, 382]
membrane <114, 269, 286> (<269>, the enzyme contains membrane localization signals [483]; <114,286>, phosphorylation of the hydrophobic motif at the extreme C terminus of PKB γ may facilitate translocation of the kinase to the membrane [225]) [483, 225]
perinuclear space <164> [308]
plasma membrane <145> (<145>, stimulation by phorbol ester causes weak translocation of δIII-GFP from the cytosol to the plasma membrane [286]) [286]
ribosome <203> [379, 380]
ribosome <14> (<14>, 54 S subunit of the yeast mitochondrial ribosome [29]) [29]
Additional information <245> (<245>, treatment of rat mammary tumor cells with serum caused hyperphosphorylation of endogenous SGK, and promoted translocation to the nucleus [442]) [442]

Purification

<48> (expression in COS 7 cells [106]) [106]
<110> [212]
<113> [224]
<135> [264]
<137> (partial purification of the PKC-zeta isoenzyme [268]) [268]
<145> (partial [290]) [290]
<146> (partial [290]) [290]
<205> (recombinant enzyme [205]) [382]
<243> (partial [268]) [268]
<272> [486]
<278> (partial [429]) [429]

Crystallization

<8> (crystal structures of catalytic subunit of cAMP-dependent protein kinase in complex with isoquinolinesulfonyl protein kinase inhibitors 1-(5-isoquinolinesulfonyl)-2-methylpiperazine, N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide and N-[2-(*p*-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide [13]; crystal structure of the protein kinase catalytic subunit with staurosporine bound to the adenosine pocket [14]) [13, 14]
<110> (crystal structure of the cys2 activator-binding domain of protein kinase C δ in complex with phorbol ester [210]) [210]
<145> (crystal structure of PKC-δ C_2 domain. Structural elements unique to this C_2 domain include a helix and a protruding β hairpin which may contribute basic sequences to a membrane-interaction site [288]) [288]

Cloning

<6> (expression in COS cells [6]) [6]
<7> (cDNA of the two isoforms of bovine cGMP-dependent protein kinase [11]) [11]
<9> (isolation of a full-length cDNA clone coding for C β 2 isoform of the bovine C-subunit [17]) [17]
<11> [24]
<12> (characterization of genomic clones coding for the C α and C β subunits [25]; isolation of a full-length cDNA clone encoding the C β catalytic subunit of cAMP-dependent protein kinase from a brain cDNA library [27]) [25, 27]
<13> [26]
<27> [68]
<30> (characterization of the human gene encoding the type I α and type I β cGMP-dependent protein kinase [77]) [77]
<33> [69]
<34> [85]
<36> [11]
<37> [89]
<38> (expression in COS-7 cells [90]) [90]
<40> [93, 94]
<41> [93]

<44> (β ARK locus segregated with the long arm of chromosome 11, centromeric to 11q13 [98]; cloning and sequencing [99]) [98, 99]
<52> (isolation of a full length cDNA clone encoding the C α type catalytic subunit of cAMP-dependent protein kinase [108]) [108]
<53> [109]
<58> (isolation of cDNA [117]; expression of the catalytic subunit DdPK3 in Escherichia coli [118]) [117, 118]
<59> (expression in COS7 cells [120]) [120]
<61> [122, 123]
<62> [124]
<66> (expressed in Sf9 cells [130]) [130]
<70> [133, 134]
<73> [77, 140]
<76> [148]
<84> (expression in COS-1 cells [161]) [161]
<86> [148]
<88> [166]
<89> [167]
<95> [176]
<98> [179]
<109> (expression of mutant enzymes in COS cells [201]; wild-type and mutant enzymes overexpressed in COS cells [202]; isolation of cloned mouse protein kinase C β-II cDNA [203]; expression in COS cells [208]) [201, 202, 206, 208]
<109> (isolation of cDNA clones encoding protein kinase C [205]) [205]
<110> (PKCδII expressed in COS-1 cells [191]) [191]
<111> [218]
<113> (characterization of the gene [192]) [192]
<113> (expression in COS cells [224]) [222, 223, 224]
<114> [227, 228]
<115> (GRK7 [189]) [189]
<116> [190, 229]
<122> [241]
<124> [242]
<137> (expression in recombinant baculovirus-infected insect cells [268]) [268]
<138> (structure and nucleotide sequence of a Drosophila melanogaster protein kinase C gene [269]) [269]
<140> (cDNA sequence encoding mouse PKC-γ isolated from a C57BL/6 brain cDNA library [273]) [273]
<140> (expression in COS cells [208]) [208]
<141> (the 5' segment of the gene for protein kinase C β is cloned from a human leukocyte genomic library in EMBL3 bacteriophage [277]) [276, 277]
<145> (cDNA cloning of an alternative splicing variant of protein kinase C δ, expression of truncated form of PKC δIII fused to green fluorescent protein in CHO-K1 cells [286]; expressed in COS 7 cells [290]) [286, 290, 291]
<203> (isolation of cDNA [378]) [378]

<216> [399, 400]
<234> [429]
<236> [222, 224]
<238> (expression in COS1 cells transfected with an nPKC theta cDNA expression plasmid [433]) [433]
<239> (protein kinase C-ε E1 and E2, expression in Sf9 cells, the recombinant protein displays protein kinase C activity and phorbol ester binding activity [434]) [434]
<241> (expressed in insect cells via a baculovirus expression vector, a 75000 Da protein is synthesized which, unlike other PKC isoforms, does not bind phorbol ester, even at very high concentrations [436]) [436]
<242> (expression in COS cells [437]) [437, 438]
<243> (expression in recombinant baculovirus-infected insect cells, overexpression in NIH 3T3 cells or insect cells [268]; isolation of cDNA [439]) [268, 439]
<244> (expression in the baculovirus insect-cell expression system [441]) [441]
<248> (expression in COS-1 cells [450]) [450]
<255> (expression in COS cells [463]) [400, 463]
<256> [400]
<258> (expression in COS1 cells [469]; expression in COS7 cells [470]) [469, 470]
<259> (expression in COS1 cells [469]) [469]
<260> [473]
<261> [473]
<267> (isolation of cDNA [480]) [480]
<268> (COS cells transfected with the PKC lambda expression plasmid [481]) [481]
<269> (bacterially expressed catalytic domain of PKD [483]) [483]
<273> [487]
<274> (DNA sequences encoding the rat Rsk-1 S6 kinase modified by insertion of a peptide epitope at the polypeptide aminoterminus, expressed in COS cells [488]) [488]
<275> (expression in COS cells [489]) [489]
<278> [429]
<283> [498, 499]
<286> [228]

Engineering

M24L <171> (<171>, mutation in the α I polypeptide suppresses synthesis of the α II polypeptides [327]) [327]
M24T <171> (<171>, mutation in the α I polypeptide suppresses synthesis of the α II polypeptides [327]) [327]
S442X <245> (<245>, mutation of putative phosphorylation sites at Thr256 and Ser422 inhibited SGK activation [442]) [442]
S79D <97> (<97>, replacement of an autophosphorylated Ser79 of cGKIβ with an aspartic acid results in a mutant kinase with constitutive kinase ac-

tivity in vitro and in vivo. The cGKIβS79D mutant localized to the cytoplasm and is only a weak activator of CRE-dependent gene transcription [178]) [178]
T256A <107> (<107>, the conditional IPTG inducible expression of wild type Sgk, but not of the kinase dead mutant T256A Sgk, protects Con8 mammary epithelial tumor cells from serum starvation-induced apoptosis [181]) [181]
T256A/S422A <107> (<107>, unlike the wild-type enzyme the phosphorylation site mutant has no effect on cell survival [181]) [181]
T256X <245> (<245>, mutation of putative phosphorylation sites at Thr256 and Ser422 inhibited SGK activation [442]) [442]
T474F <113> (<113>, 55% inhibition of Akt activation [187]) [187]
T500E <109> (<109>, expression as a catalytically active protein kinase C in COS cells [201]) [201]
T500V <109> (<109>, expression as a catalytically inactive protein kinase C in COS cells [201]) [201]
Additional information <114> (<114>, phosphorylation of Ser472 and phosphorylation of Thr305 appears to contribute to the activation of Akt-3 because mutation of both these residues to aspartate increases the catalytic activity of Akt-3, whereas mutation to alanine inhibits activation [227]) [227]
Additional information <185> (<185>, mutant, gprk2(6936) disrupts expression of a putative member of the GRK family, the G protein-coupled receptor kinase 2 gene Gprk2. This mutation affects Gprk2 gene expression in the ovaries and renders mutant females sterile. The mutant eggs contain defects in several anterior eggshell structures that are produced by specific subsets of migratory follicle cells. In addition, rare eggs that become fertilized display severe defects in embryogenesis [349]) [349]
Additional information <248> (<248>, a CTG triplet repeat undergoes expansion in myotonic dystrophy patients. This sequence is highly variable in the normal population, unaffected individuals have been 5 and 27 copies, myotonic dystrophy patients are minimally affected have at least 50 repeats, more severely affected patients have expansion of the repeat containing segment up to several kilobase pairs [454]) [454]

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